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TRANSMITTAL FORM

Application Serial Number	09/754,831
Filing Date	January 3, 2001
First Named Inventor	Oppermann
Group Art Unit	1646
Examiner Name	Kemmerer, Elizabeth
Attorney Docket No.	STK-008CN
Patent No.	Not applicable
Issue Date	Not applicable

ENCLOSURES *(check all that apply)*

- ☐ Fee Transmittal Form
  - ☐ Check Attached
  - ☐ Copy of Fee Transmittal Form
- ☐ Amendment/Response
  - ☐ Preliminary
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
  - ☐ Letter to Official Draftsperson including Drawings [Total Sheets _____]
- ☐ Petition for Extension of Time
- ☐ Information Disclosure Statement
  - ☐ Form PTO-1449
  - ☐ Copies of IDS Citations
- ☐ Certified Copy of Priority Document(s)
- ☐ Sequence Listing submission
  - ☐ Paper Copy/CD
  - ☐ Computer Readable Copy
  - ☐ Statement verifying identity of above
- ☐ Copy of Notice to File Missing Parts of Application
- ☐ Formal Drawing(s)
- ☐ Request For Continued Examination (RCE) Transmittal
- ☐ Power of Attorney (Revocation of Prior Powers)
- ☐ Terminal Disclaimer
- ☐ Executed Declaration and Power of Attorney for Utility or Design Patent Application
- ☐ Small Entity Statement
- ☐ CD(s) for large table or computer program
- ☐ Amendment After Allowance
- ☐ Request for Certificate of Correction
  - ☐ Certificate of Correction (in duplicate)
- ☐ Notice of Appeal to Board of Patent Appeals and Interferences
- ☐ Appeal Brief (in triplicate)
- ☐ Status Inquiry
- ☒ Return Receipt Postcard
- ☐ Certificate of First Class Mailing under 37 C.F.R. 1.8
- ☐ Certificate of Facsimile Transmission under 37 C.F.R. 1.8
- ☒ Additional Enclosure(s) *(please identify below)*
  - Form PTOL-85B
  - Transmittal of Issue Fee
  - Exhibit A
  - Check in the amount of $1,700.00

CORRESPONDENCE ADDRESS

Direct all correspondence to: Patent Administrator
Kirkpatrick & Lockhart Nicholson Graham LLP
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SIGNATURE BLOCK

Respectfully submitted,

Date: January 13, 2006
Reg. No. 51,551
Tel. No.: (617) 261-3198
Fax No.: (617) 261-3175

Fangli Chen, Ph.D.
Agent for Applicants
Kirkpatrick & Lockhart Nicholson Graham LLP
75 State Street
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT(S):	Oppermann *et al.*	CONFIRMATION NO.:	3498
SERIAL NO.:	09/754,831	GROUP NO.:	1646
FILING DATE:	January 3, 2001	EXAMINER	Kemmerer, Elizabeth
TITLE:	Nucleic Acid Molecules Encoding Osteogenic Proteins		

TRANSMITTAL OF ISSUE FEE

MAIL STOP ISSUE FEE
Commissioner for Patents
Alexandria, VA 22313-1450

Sir:

In response to the Notice of Allowance and Fee(s) Due mailed on October 18, 2005, attached please find:

(a) Fee(s) Transmittal (Form PTOL-85B); and

(b) a check in the amount of $1,700.00 for payment of Issue Fee and Publication Fee.

Applicants notice that the Title of Invention is listed as "Osteogenic Devices" on the Notice of Allowance. Applicants submit that the title of invention was amended in the response filed on January 7, 2005, a copy of which is attached herewith as Exhibit A with relevant text highlighted. The amended title should read "Nucleic Acid Molecules Encoding Osteogenic Proteins." Accordingly, Applicants respectfully request that the Notice of Allowance be amended to reflect the correct title and the correct title "Nucleic Acid Molecules Encoding Osteogenic Proteins" be used on the issued patent.

Applicants believe no other fees are due with the submission of this paper. Should Applicants be in error, please consider this a conditional authorization to charge Deposit Account No. 50-1721.

The Examiner is invited to contact the undersigned to discuss any issues relating to the application.

Respectfully submitted,

Date: January 13, 2006
Reg. No. 51,551

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PATENT
Attorney Docket No. STK-008CN

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS:	Oppermann *et al.*		
SERIAL NO.:	09/754,831	GROUP NO.:	1646
FILING DATE:	January 3, 2001	EXAMINER:	E. C. Kemmerer
TITLE:	NUCLEIC ACID MOLECULES ENCODING OSTEOGENIC PROTEINS (As Amended)		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE

Dear Sir:

This paper is responsive to the Office action for the above-identified patent application, mailed from the U.S. Patent and Trademark Office on October 4, 2004. Applicants believe that no petition or fee is required for entry and consideration of this paper. If any petition or fee is required, please consider this a conditional petition for any required extension of time, and a conditional authorization to charge any required fee to Deposit Account No. 20-0531.

Amendments to the Specification begin on page 2 of this paper.

Amendments to the Claims are reflected in the listing of claims, which begins on page 4 of this paper.

Remarks begin on page 7 of this paper.

AMENDMENTS TO THE SPECIFICATION

On page 1, please delete the title "OSTEOGENIC DEVICES" and replace with the following title:

NUCLEIC ACID MOLECULES ENCODING OSTEOGENIC PROTEINS

On pages 9-11, please replace the paragraph starting with "In one preferred aspect" and ending with "such activity" with the following amended paragraph:

In one preferred aspect, these proteins comprise species of the generic amino acid sequences (SEQ ID NO: 3 and SEQ ID NO: 4, respectively):

```
1         10         20         30         40         50
      LXVXFXDXGWXXWXXXPXGXXAXYCXGXCXXPXXXXXXXXNHAXX
          60         70         80         90        100
QXXVXXXNXXXXPXXCCXPXXXXXXXXLXXXXXXXVXLXXYXXMXVXXCXCX

or
1         10         20         30         40         50
CXXXXLXVXFXDXGWXXWXXXPXGXXAXYCXGXCXXPXXXXXXXXNHAXX
          60         70         80         90        100
QXXVXXXNXXXXPXXCCXPXXXXXXXXLXXXXXXXVXLXXYXXMXVXXCXCX
```

where the letters indicate the amino acid residues of standard single letter code, and the Xs represent amino acid residues. Preferred amino acid sequences within the foregoing generic sequences are (SEQ ID NO: 5 and SEQ ID NO: 6, respectively):

```
          10         20         30         40         50
      LYVDFRDVGWNDWIVAPPGYHAFYCHGECPFPLADHLNSTNHAIV
       K S S L  QE VIS E FD Y  E A AY MPESMKAS   VI
       F E K I  DN     L    N  S   Q  ITK F P    TL
           A    S      K

          60         70         80         90        100
QTLVNSVNPGKIPKACCVPTELSAISMLYLDENENVVLKNYQDMVVEGCGCR
~~SI HAI SEQV EP  A EQMNSLAI FFNDQDK I RK EE T DA H H~~
 SI HAI SEQV EP  A EQMNSLAI FFNDQDK I RK EE T DA H H
    RF    T   S     K DPV V  Y N S     H RN   RS
     N    S                    K       P    E
```

and

```
         10         20         30         40         50
CKRHPLYVDFRDVGWNDWIVAPPGYHAFYCHGECPFPLADHLNSTNHAIV
 RRRS K S S L  QE VIS E FD Y  E A AY MPESMKAS   VI
   KE F E K I  DN     L    N  S   Q  ITK F P    TL
    Q     A    S       K

         60         70         80         90        100
QTLVNSVNPGKIPKACCVPTELSAISMLYLDENENVVLKNYQDMVVEGCGCR
 SI HAI SEQV EP  A EQMNSLAI FFNDQDK I RK EE T DA H H
    RF    T  S     K DPV V  Y N S     H RN   RS
     N    S                      K       P     E
```

Wherein each of the amino acids arranged vertically at each position in the sequence may be used alternatively in various combinations. Note that these generic sequences have 6 and preferably 7 cysteine residues where inter- or intramolecular disulfide bonds can form, and contain other critical amino acids which influence the tertiary structure of the proteins. These generic structural features are found in previously published sequences, none of which have been described as capable of osteogenic activity, and most of which never have been linked with such activity.

AMENDMENTS TO THE CLAIMS

The following listing of claims replaces all prior versions of the claims pending in this application:

Listing of Claims

1-80. (Canceled).

81. (Previously presented) An isolated nucleic acid molecule comprising the nucleic acid sequence:

(a)

CTGTATGTCAGCTTCCGAGACCTGGGCTGGCAGGACTGGATCATCGCGCCTG
AAGGCTACGCGCGCTACTACTGTGAGGGGGAGTGTGCCTTCCCTCTGAACTC
CTACATGAACGCCACCAACCACGCCATCGTGCAGACGCTGGTCCACTTCATC
AACCCGGAAACGGTGCCCAAGCCCTGCTGTGCGCCCACGCAGCTCAATGCCA
TCTCCGTCCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACAGA
AACATGGTGGTCCGGGCCTGTGGCTGCCACTAGCTCCT (nucleotides 16-314 of SEQ ID NO: 42), or

(b) encoding an amino acid sequence:

LYVSFRDLGWQDWIIAPEGYAAYYCEGECAFPLNSYMNATNHAIVQTLV
HFINPETVPKPCCAPTQLNAISVLYFDDSSNVILKKYRNMVVRACGCH
(SEQ ID NO: 39), or a conservative amino acid variant thereof,

wherein said nucleic acid sequence encodes a protein competent to induce bone and cartilage in a mammal.

82. (Previously presented) The isolated nucleic acid molecule of claim 81 comprising the nucleic acid sequence

TGTAAGAAGCACGAGCTGTATGTCAGCTTCCGAGACCTGGGCTGGCAGGACT
GGATCATCGCGCCTGAAGGCTACGCGCGCTACTACTGTGAGGGGGAGTGTGC
CTTCCCTCTGAACTCCTACATGAACGCCACCAACCACGCCATCGTGCAGACG

CTGGTCCACTTCATCAACCCGGAAACGGTGCCCAAGCCCTGCTGTGCGCCCA CGCAGCTCAATGCCATCTCCGTCCTCTACTTCGATGACAGCTCCAACGTCATC CTGAAGAAATACAGAAACATGGTGGTCCGGGCCTGTGGCTGCCACTAGCTCC T (SEQ ID NO: 42),

or encoding an amino acid sequence:

CKKHELYVSFRDLGWQDWIIAPEGYAAYYCEGECAFPLNSYMNATNHAIVQTL VHFINPETVPKPCCAPTQLNAISVLYFDDSSNVILKKYRNMVVRACGCH (amino acids 6-107 of SEQ ID NO: 9).

83. (Currently amended) The isolated nucleic acid molecule of claim 81 or 82, wherein said protein competent to induce bone and cartilage further comprises

(a) a pair of unglycosylated polypeptide chains, each of said unglycosylated polypeptide chains having a molecular weight of about 14 kDa to 16 kDa, as determined by polyacrylamide gel electrophoresis under reducing conditions; or

(b) an unglycosylated dimeric protein having a molecular weight of about 27 kDa, as determined by polyacrylamide gel electrophoresis under non-reducing conditions.

84. (Cancelled)

85. (Cancelled)

86. (Cancelled)

87. (Currently amended) An isolated host cell transformed with the nucleic acid molecule of ~~any one of~~ claims 81, or 82~~, 84, 85, or 86~~.

88. (Currently amended) ~~A~~The isolated host cell of claim 87, wherein said cell is a prokaryotic or an eukaryotic cell.

89. (Currently amended) The isolated host cell of claim 88, wherein said prokaryotic cell is an E.coli cell, and said eukaryotic cell is a Saccharomyces cell or a mammalian cell.

90. (Currently amended) The isolated nucleic acid molecule of any one of claims 81-~~86~~83, wherein the nucleic acid is DNA.

91. (Currently amended) The isolated host cell of any one of claims 87-89, wherein the nucleic acid is DNA.

REMARKS

Claims 81-83, 85, and 87-91 were pending in this application. Claims 84 and 86 were withdrawn from consideration as being directed to a non-elected invention. Claims 84, 85 and 86 are now cancelled without prejudice to Applicants' right to prosecute their subject matter in the present application and in related applications. Claims 83 and 87-91 are currently amended without any intent of disclaiming equivalents thereof. Accordingly, claims 81-83 and 87-91 are pending and presented for consideration.

Specification amendments

Applicants have amended the title to be indicative of the invention to which the pending claims are directed. In addition, Applicants have amended the specification to correct a hand-written notation and a typographical error. Support for the amendment is found in the specification at least, for example, at page 10, line 31, and at page 62, line 40. Applicants respectfully submit that the amendments to the specification introduce no new matter.

Claim amendments

Support for the amendment to claim 83 can be found in the specification as originally filed at least, for example, in the paragraph bridging pages 43 and 44, and in Figure 5 and accompanying text. Support for the amendment to claims 87-89 and 91 can be found in the specification as originally filed at least, for example, at page 60, the second paragraph. Claims 87, 88, 90 and 91 have also been amended to delete the reference to the cancelled claims and to correct informalities. Applicants respectfully submit that the amendments to the claims introduce no new matter.

Sequence Rules

The Office action objects to the application as being not fully in compliance with the sequence rules, 37 C.F.R. §§ 1.821-1.825. Specifically, the Office action alleges that the specification does not include sequence identifiers. Applicants submit that a Preliminary Amendment was filed on September 10, 2001, to introduce sequence identifiers into the specification. A copy of the Preliminary Amendment filed on September 10, 2001, is attached as

Exhibit A. Applicants respectfully request that the Preliminary Amendment of September 10, 2001, be entered and the objection be reconsidered and withdrawn.

Objection to the specification

The Office action objects to the specification for containing hand-written notations. The Office action also objects to the title of the invention for not being descriptive. Applicants have amended the specification and the title to overcome the objections. Accordingly, Applicants request reconsideration and withdrawal of the objection to the specification.

Claim objections

The Office action objects to claims 87-91 for depending from the non-elected inventions. Applicants have amended claims 87-91 to delete the reference to the non-elected inventions. Accordingly, Applicants request reconsideration and withdrawal of the objection to claims 87-91.

Claim Rejections Under 35 U.S.C. § 112, second paragraph

Claims 83, 85, 87-89 and 91 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Specifically, the Office action alleges that claim 83 fails to recite the method to determine the recited molecular weight. Claim 83 has been amended to recite "(a) a pair of unglycosylated polypeptide chains, each of said unglycosylated polypeptide chains having a molecular weight of about 14 kDa to 16 kDa, as determined by polyacrylamide gel electrophoresis under reducing conditions; or (b) an unglycosylated dimeric protein having a molecular weight of about 27 kDa, as determined by polyacrylamide gel electrophoresis under non-reducing conditions." In view of the amendment, Applicants request reconsideration and withdrawal of the rejection of claim 83.

The Office action alleges that the recitation "consisting essentially of" in claim 85 is not clear. Without acquiescing to the merits of the rejection and in order to speed prosecution of this application, Applicants have cancelled claim 85. In view of the cancellation of claim 85, Applicants request reconsideration and withdrawal of the rejection of claim 85.

The Office action alleges that claims 87-89 and 91 are not clear in terms of whether the claims are directed to isolated host cells or host cells in the context of multi-cellular transgenic organisms, possibly even humans. Applicants have amended the claims to recite "isolated host cell." Accordingly, Applicants request reconsideration and withdrawal of the rejection of claims 87-89 and 91.

Double Patenting

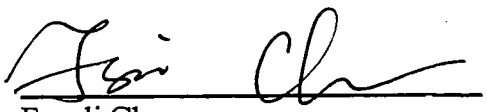
Applicants request that all double patenting rejections be held in abeyance until the presence of otherwise-allowable subject matter is acknowledged.

CONCLUSION

Claims 81-83 and 87-91 are presently pending in this application. The Examiner is invited to contact the undersigned with any questions about this paper. Early and favorable action is respectfully solicited.

Date: January 7, 2005
Reg. No. 51,551

Respectfully submitted,



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